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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,103	07/05/2002	Sandrine Lentsch Graf	01-1081	4719

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,103	GRAF ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This Office action is responsive to Applicant's amendment and response filed June 15, 2005. Claims 2-9 have been amended. Claim 1 has been cancelled. Claim 17 has been added.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. In view of Applicant's amendments and remarks the following rejections are withdrawn:

a) Rejection of claims 1-8 and 11-16 under 35 U.S.C. 103(a), pages 4-7, paragraph 6.

b) Rejection of claims 9-13 and 16 under 35 U.S.C. 103(a), pages 8-9 paragraph 7.

Rejection Maintained

4. The rejection under 35 U.S.C. 103(a) paragraph is maintained for claims 2-8 and 11-15 and newly submitted claim 17 for the reasons set forth on pages 3-4, paragraph 5 of the previous Office Action.

The rejection was on the grounds that LaPosta et al teach a liquid vaccine composition comprising a polysaccharide covalently bound to a protein (column 4, lines 60-65). LaPosta et al teach that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition (column 3, lines 10-26). LaPosta et al anticipate the claimed invention. LaPosta et al teach suitable antigens used in the vaccine include antigens from *Haemophilus influenzae, Neisseria meningitidis* and *Streptococcus pneumoniae*, Group A *Streptococcus* and Group B *Streptococcus* (column 4, lines 25-64). LaPosta et al teach that the antigens of the invention, for example, bacterial capsular polysaccharide or a fragment thereof is chemically linked to a protein carrier molecule in order to enhance immunogenicity (column 4, lines 60-64). LaPosta, et al anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's vaccine and the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the presently claimed compositions do not encompass the compositions of LaPosta et al because LaPosta et al do not store a liquid composition comprising trehalose and antigen. Applicant urges that a liquid vaccine composition will inherently undergo changes overtime and the presently claimed liquid vaccine compositions are different from LaPosta et al. Applicant urges that LaPosta et al cannot anticipate the present claims.

Applicant's arguments filed June 15, 2005 have been fully considered but they are not persuasive. The claims are directed to a product, a liquid vaccine composition. LaPosta et al teach a liquid composition comprising an antigen (polysaccharide bound to a protein carrier) and trehalose. The claim limitation "storing the liquid vaccine in the liquid state" is a process limitation in a product claim.

To address Applicant's comments regarding liquid compositions it should be noted that the prior art reference teaches liquid compositions as well as lyophilized compositions. Applicant has provided no side-by-side comparison to show that the liquid compositions of the prior art differ from the claimed liquid vaccine compositions. Therefore, LaPosta et al anticipate the claimed invention.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2-8, 11-15 and 17 are rejected under 35 U.S.C. 103(a) unpatentable over Anderson et al (*U.S. Patent No. 5,097,020 published March 17, 1992)* in view of Samaritani (*WO 96/29095 published September 26, 1996)* and further in view of Sola-Penna et al *(Archives of Biochemistry and Biophysics, Vol. 360, No. 1, December 1, 1998, p. 10-14).*

Claims 2-8, 11-15 and 17 are drawn to a liquid vaccine composition prepared by a process comprising (a) combining in a liquid (a) trehalose with (b) at least one antigen consisting of a polysaccharide bound to a carrier protein to form a liquid vaccine composition and (b) storing the liquid vaccine composition in the liquid state.

Anderson et al teach vaccine comprising covalent attachment of capsular polymer fragment derived from bacterial capsular polymers to bacterial toxoids (column 2, lines 58-64). Anderson et al teach that suitable carrier proteins of the inventions include diphtheria and tetanus toxoids (columns 5, lines 29-36). Anderson et al teach that vaccine of the invention include vaccines against systemic infections caused by the pathogens *Haemophilus influenzae* type b, *E. coli*, pneumococcus, meningococcus, streptococcus and pseudomonas (column 6, lines 59-65). Anderson et al teach that the regulation of any reaction parameter, e.g. time, temperature, pH, etc. which affects the reactivity or rate of reaction will alter the final composition and structure of the conjugate (column 4, lines 45-49). Anderson et al teach that the vaccines of the invention have been lyophilized (column 18, lines 35-40). Anderson et al teach that the conjugates of the invention appear to convert into macromolecular aggregates after preparation (column 13, lines 67-68 and column 14, lines 1-2).

Anderson et al do not teach retaining the vaccine composition in liquid form nor does Anderson et al teach the addition of a non-reducing sugar.

Samaritani teaches that pharmaceutical compositions can be maintained in the liquid form to avoid processes such as lyophilization (see the Abstract). Samaritani

teaches that non-reducing sugars are used to stabilized these compositions in liquid form (see the Abstract).

Samaritani does not teach the non-reducing sugar trehalose.

Sola-Penna et al teach that trehalose is more effective at stabilizing compositions than other sugars (see the Abstract and the Title). Sola-Penna et al teach that trehalose is the best stabilizer of macromolecules because trehalose has the ability to protect these molecules from thermal inactivation (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to use trehalose to stabilize liquid composition comprising an antigen (polysaccharide bound to a carrier molecule) formulated in a liquid composition because Samaritani that non-reducing sugars can be used to stabilize pharmaceutical compositions that are maintained in the liquid state and Sola-Penna et al teach that trehalose is the best non-reducing sugar that can be used to stabilize of macromolecules. It would be expected barring evidence to the contrary that trehalose would be effective in stabilizing pharmaceutical compositions that are maintained in the liquid state because the prior art has shown that non-reducing sugars are effective at stabilizing pharmaceutical compositions in the liquid state.

6. Claims 9-10 and 16 are rejected under 35 U.S.C. 103(a) unpatentable over Samaritani (*WO 96/29095 published September 26, 1996)* in view of Sola-Penna et al *(Archives of Biochemistry and Biophysics, Vol. 360, No. 1, December 1, 1998, p. 10-14)* and further in view of Anderson et al (*U.S. Patent No. 5,097,020 published March 17, 1992).*

Samaritani teaches a method of preserving the immunogencity of a pharmaceutical composition maintained in liquid form over time by using non-reducing sugars to stabilize these compositions (see the Abstract and page 1).

Samaritani does not teach the non-reducing sugar trehalose.

Sola-Penna et al teach that trehalose is more effective at stabilizing compositions than other sugars (see the Abstract and the Title). Sola-Penna et al teach that trehalose is the best stabilizer of macromolecules because trehalose has the ability to protect these molecules from thermal inactivation (see the Abstract).

Samaritani nor Sola-Penna et al teach vaccine compositions comprising an antigen consisting of a polysaccharide bound to a carrier protein.

Anderson et al teach vaccine comprising covalent attachment of capsular polymer fragment derived from bacterial capsular polymers to bacterial toxoids (column 2, lines 58-64). Anderson et al teach that suitable carrier proteins of the inventions include diphtheria and tetanus toxoids (columns 5, lines 29-36). Anderson et al teach that vaccine of the invention include vaccines against systemic infections caused by the pathogens *Haemophilus influenzae* type b, *E. coli*, pneumococcus, meningococcus, streptococcus and pseudomonas (column 6, lines 59-65). Anderson et al teach that the

regulation of any reaction parameter, e.g. time, temperature, pH, etc. which affects the reactivity or rate of reaction will alter the final composition and structure of the conjugate (column 4, lines 45-49). Anderson et al teach that the vaccines of the invention have been lyophilized (column 18, lines 35-40). Anderson et al teach that the conjugates of the invention appear to convert into macromolecular aggregates after preparation (column 13, lines 67-68 and column 14, lines 1-2).

It would be *prima facie* obvious at the time the invention was made to use trehalose to stabilize a liquid vaccine composition comprising an antigen (polysaccharide bound to a carrier molecule) used in a method to preserve the immunogenicity of the vaccine composition over time because Samaritani that non-reducing sugars can be used to stabilize pharmaceutical compositions that are maintained in the liquid state and Sola-Penna et al teach that trehalose is the best stabilizer of macromolecules. It would be expected barring evidence to the contrary that trehalose would be effective in stabilizing pharmaceutical compositions that are maintained in the liquid state because Samaritani teaches that non-reducing sugars can stabilized compositions in the liquid state to avoid processes such as lyophilization thereby making the compositions readily injectable.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action.. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Status of Claims

8. No claims are allowed.

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
August 16, 2005

NITA MINNIFIELD
PRIMARY EXAMINER
8/17/05